

WHAT IS CLAIMED IS:

1. An isolated polynucleotide comprising a sequence selected from the group comprising:
 - (i) the nucleotide sequence of SEQ ID NO:4;
 - (ii) a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:1;
 - (iii) a nucleotide sequence encoding an ELR-CXC chemokine antagonist comprising an amino acid sequence substantially equivalent to a wild-type bovine CXCL8 sequence, wherein
 - (a) the amino acid sequence of the antagonist starts at amino acid residue Thr3,
 - (b) Lys11 of the wild-type sequence is substituted with Arg in the amino acid sequence of the antagonist, and
 - (c) Gly31 of the wild-type sequence is substituted with Pro in the in the amino acid sequence of the antagonist;
 - (iv) a nucleotide sequence encoding an ELR-CXC chemokine antagonist comprising an amino acid sequence substantially equivalent to a wild-type bovine CXCL8 sequence, wherein
 - (a) the amino acid sequence of the antagonist starts at amino acid residue Thr3,
 - (b) Lys11 of the wild-type sequence is substituted with Arg in the amino acid sequence of the antagonist,
 - (c) Gly31 of the wild-type sequence is substituted with Pro in the in the amino acid sequence of the antagonist, and

- (d) Pro32 of the wild-type sequence is substituted with Gly in the amino acid sequence of the antagonist; and
- (v) a nucleotide sequence encoding an ELR-CXC chemokine antagonist comprising an amino acid sequence substantially equivalent to a wild-type bovine CXCL8 sequence, wherein
 - (a) the amino acid sequence of the antagonist starts at amino acid residue Thr3,
 - (b) Lys11 of the wild-type sequence is substituted with Arg in the amino acid sequence of the antagonist,
 - (c) Thr12 of the wild-type sequence is substituted with Ser in the amino acid sequence of the antagonist,
 - (d) His13 of the wild-type sequence is substituted with Phe in the amino acid sequence of the antagonist, and
 - (e) Gly31 of the wild-type sequence is substituted with Pro in the in the amino acid sequence of the antagonist.
- 2. An isolated polynucleotide comprising the complement of the polynucleotide of claim 1.
- 3. An isolated polynucleotide encoding a polypeptide capable of high-affinity binding to CXCR1 and CXCR2 receptors in a mammalian inflammatory cell so as to inhibit activation of the inflammatory cell.
- 4. A polypeptide encoded by the polynucleotide of claim 1.
- 5. A polypeptide encoded by the polynucleotide of claim 3.
- 6. A host cell genetically engineered to contain the polynucleotide of claim 1.

7. The host cell of claim 6, selected from the group comprising bacteria, yeast, protozoa, fungi, algae, plant cells, and animal cells.
8. A viral host genetically engineered to contain the polynucleotide of claim 1.
9. A host cell genetically engineered to contain the polynucleotide of claim 3.
10. The host cell of claim 9, selected from the group comprising bacteria, yeast, fungi, algae, plant cells, and animal cells.
11. A viral host genetically engineered to contain the polynucleotide of claim 3.
12. A host cell genetically engineered to contain the polynucleotide of claim 1 operatively associated with a regulatory sequence that controls expression of the polynucleotide in the host.
13. The host cell of claim 12, selected from the group comprising bacteria, yeast, fungi, algae, plant cells, and animal cells.
14. A viral host genetically engineered to contain the polynucleotide of claim 1 operatively associated with a regulatory sequence that controls expression of the polynucleotide in the host.
15. A host cell genetically engineered to contain the polynucleotide of claim 3 operatively associated with a regulatory sequence that controls expression of the polynucleotide in the host.
16. The host cell of claim 15, selected from the group comprising bacteria, yeast, protozoa, fungi, algae, plant cells, and animal cells.

17. A viral host genetically engineered to contain the polynucleotide of claim 3 operatively associated with a regulatory sequence that controls expression of the polynucleotide in the host.
18. A vector comprising the polynucleotide of claim 1.
19. An expression vector comprising the polynucleotide of claim 1 and being operatively associated with a regulatory sequence that controls expression of the polynucleotide.
20. A host cell containing the expression vector of claim 19.
21. The host cell of claim 20, selected from the group comprising bacteria, protozoa, yeast, fungi, algae, plant cells, and animal cells.
22. A viral host containing the expression vector of claim 19.
23. An ELR-CXC chemokine antagonist comprising an amino acid sequence substantially equivalent to a wild-type bovine CXCL8 sequence, said amino acid sequence further comprising differences from the wild-type amino acid sequence selected from the group comprising:
 - (i) a truncation of the first two amino acid residues of the antagonist sequence such that it starts at amino acid residue Thr3, a substitution of Lys11 of the wild-type sequence with Arg in the amino acid sequence of the antagonist, and a substitution of Gly31 of the wild-type sequence with Pro in the amino acid sequence of the antagonist;
 - (ii) a truncation of the first two amino acid residues of the antagonist sequence such that it starts at amino acid residue Thr3, a substitution of Lys11 of the wild-type

sequence with Arg in the amino acid sequence of the antagonist, a substitution of Gly31 of the wild-type sequence with Pro in the in the amino acid sequence of the antagonist, and a substitution of Pro32 of the wild-type sequence with Gly in the amino acid sequence of the antagonist; and

- (iii) a truncation of the first two amino acid residues of the antagonist sequence such that it starts at amino acid residue Thr3, a substitution of Lys11 of the wild-type sequence with Arg in the amino acid sequence of the antagonist, a substitution of Thr12 of the wild-type sequence with Ser in the amino acid sequence of the antagonist, a substitution of His13 of the wild-type sequence with Phe in the amino acid sequence of the antagonist, and a substitution of Gly31 of the wild-type sequence with Pro in the in the amino acid sequence of the antagonist.

24. Use of the chemokine of claim 23 in treating a CXC chemokine-mediated pathology wherein the chemokine binds to CXCR1 or CXCR2 receptors in a mammal.
25. A method of treating an ELR-CXC chemokine-mediated pathology wherein the chemokine binds to CXCR1 or CXCR2 receptors in a mammal, comprising administering to said mammal an effective amount of the chemokine of claim 23.
26. The method of claim 25, wherein the mammal is a bovid.
27. The method of claim 25, wherein the mammal is a human.
28. The method of claim 25, wherein the compound is administered to the mammal by means selected from the group comprising intravenous delivery, intradermal delivery, and subcutaneous delivery.

29. The method of claim 25, wherein the pathology is selected from the group comprising ischemia-reperfusion injury, endotoxemia-induced acute respiratory distress syndrome, immune complex-type glomerulonephritis, bacterial pneumonia, and mastitis.
30. A method of producing the polypeptide of claim 4 comprising:
- (i) introducing a gene encoding said polypeptide into a host cell;
 - (ii) growing said host cell;
 - (iii) accumulating said polypeptide;
 - (iv) preparing an extract containing said polypeptide;
 - (v) purifying said polypeptide.
31. A method of claim 30, wherein said host cell is selected from the list consisting of bacteria, yeast, fungi, algae, protozoa, plant cells and animal cells.
32. A method of producing the polypeptide of claim 6 comprising:
- (i) introducing a gene encoding said polypeptide into a host cell;
 - (ii) growing said host cell;
 - (iii) accumulating said polypeptide;
 - (iv) preparing an extract containing said polypeptide;
 - (v) purifying said polypeptide.
33. A method of claim 32, wherein said host cell is selected from the list consisting of bacteria, yeast, fungi, algae, protozoa, plant cells and animal cells.
34. A method of producing the polypeptide of claim 4 in a plant comprising:

- (i) introducing a gene encoding said polypeptide into said plant;
 - (ii) growing said plant;
 - (iii) accumulating said polypeptide in said plant;
 - (iv) preparing an extract containing said polypeptide;
 - (v) purifying said polypeptide.
35. A method of producing the polypeptide of 4 in an animal comprising:
- (i) introducing a gene encoding said polypeptide into said animal;
 - (ii) growing said animal;
 - (iii) accumulating said polypeptide in said animal;
 - (iv) preparing an extract containing said polypeptide;
 - (v) purifying said polypeptide.
36. A method of producing the polypeptide of claim 6 in a plant comprising:
- (i) introducing a gene encoding said polypeptide into said plant;
 - (ii) growing said plant;
 - (iii) accumulating said polypeptide in said plant;
 - (iv) preparing an extract containing said polypeptide;
 - (v) purifying said polypeptide.
37. A method of producing the polypeptide of 6 in an animal comprising:
- (i) introducing a gene encoding said polypeptide into said animal;
 - (ii) growing said animal;

- (iii) accumulating said polypeptide in said animal;
 - (iv) preparing an extract containing said polypeptide;
 - (v) purifying said polypeptide.
38. A gene fusion comprising an affinity handle and a polynucleotide comprising a sequence selected from the group comprising:
- (i) the nucleotide sequence of SEQ ID NO:4;
 - (ii) a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:1;
 - (iii) a nucleotide sequence encoding an ELR-CXC chemokine antagonist comprising an amino acid sequence substantially equivalent to a wild-type bovine CXCL8 sequence, wherein
 - (a) the amino acid sequence of the antagonist starts at amino acid residue Thr3,
 - (b) Lys11 of the wild-type sequence is substituted with Arg in the amino acid sequence of the antagonist, and
 - (c) Gly31 of the wild-type sequence is substituted with Pro in the in the amino acid sequence of the antagonist;
 - (iv) a nucleotide sequence encoding an ELR-CXC chemokine antagonist comprising an amino acid sequence substantially equivalent to a wild-type bovine CXCL8 sequence, wherein
 - (a) the amino acid sequence of the antagonist starts at amino acid residue Thr3,

- (b) Lys11 of the wild-type sequence is substituted with Arg in the amino acid sequence of the antagonist,
 - (c) Gly31 of the wild-type sequence is substituted with Pro in the in the amino acid sequence of the antagonist, and
 - (d) Pro32 of the wild-type sequence is substituted with Gly in the amino acid sequence of the antagonist; and
- (v) a nucleotide sequence encoding an ELR-CXC chemokine antagonist comprising an amino acid sequence substantially equivalent to a wild-type bovine CXCL8 sequence, wherein
- (a) the amino acid sequence of the antagonist starts at amino acid residue Thr3,
 - (b) Lys11 of the wild-type sequence is substituted with Arg in the amino acid sequence of the antagonist,
 - (c) Thr12 of the wild-type sequence is substituted with Ser in the amino acid sequence of the antagonist,
 - (d) His13 of the wild-type sequence is substituted with Phe in the amino acid sequence of the antagonist, and
 - (e) Gly31 of the wild-type sequence is substituted with Pro in the in the amino acid sequence of the antagonist.

39. A gene fusion comprising an affinity handle and a polynucleotide encoding a polypeptide capable of high-affinity binding to CXCR1 and CXCR2 receptors in a mammalian inflammatory cell so as to inhibit activation of the inflammatory cell.
40. A fusion polypeptide encoded by the gene fusion of claim 38.
41. A fusion polypeptide encoded by the gene fusion of claim 39.
42. A host cell genetically engineered to contain the gene fusion of claim 38.
43. A host cell genetically engineered to contain the gene fusion of claim 39.
44. The host cell of claim 42, selected from the group comprising bacteria, yeast, protozoa, fungi, algae, plant cells, and animal cells.
45. A viral host genetically engineered to contain the gene fusion of claim 38.
46. A host cell genetically engineered to contain the gene fusion of claim 39.
47. The host cell of claim 46, selected from the group comprising bacteria, yeast, fungi, algae, plant cells, and animal cells.
48. A viral host genetically engineered to contain the gene fusion of claim 39.
49. A host cell genetically engineered to contain the gene fusion of claim 38 operatively associated with a regulatory sequence that controls expression of the gene fusion in the host.
50. The host cell of claim 49, selected from the group comprising bacteria, yeast, fungi, algae, plant cells, and animal cells.

51. A viral host genetically engineered to contain the gene fusion of claim 38 operatively associated with a regulatory sequence that controls expression of the gene fusion in the host.
52. A host cell genetically engineered to contain the gene fusion of claim 39 operatively associated with a regulatory sequence that controls expression of the gene fusion in the host.
53. The host cell of claim 52, selected from the group comprising bacteria, yeast, protozoa, fungi, algae, plant cells, and animal cells.
54. A viral host genetically engineered to contain the gene fusion of claim 39 operatively associated with a regulatory sequence that controls expression of the gene fusion in the host.
55. A vector comprising the gene fusion of claim 38.
56. An expression vector comprising the gene fusion of claim 38 and being operatively associated with a regulatory sequence that controls expression of the gene fusion.
57. A host cell containing the expression vector of claim 56.
58. The host cell of claim 57, selected from the group comprising bacteria, protozoa, yeast, fungi, algae, plant cells, and animal cells.
59. A viral host containing the expression vector of claim 56 .
- 60 ~~57~~. A vector comprising the gene fusion of claim 39.
- 61 ~~58~~. An expression vector comprising the gene fusion of claim 39 and being operatively associated with a regulatory sequence that controls expression of the gene fusion.

62 69. A host cell containing the expression vector of claim 68.

63 70. The host cell of claim 69, selected from the group comprising bacteria, protozoa, yeast, fungi, algae, plant cells, and animal cells.

64 71. A viral host containing the expression vector of claim 68 .

65 72. An ELR-CXC chemokine antagonist comprising an amino acid sequence substantially equivalent to a wild-type bovine CXCL8 sequence, said amino acid sequence further comprising differences from the wild-type amino acid sequence selected from the group comprising:

- (i) a truncation of the first two amino acid residues of the antagonist sequence such that it starts at amino acid residue Thr3, a substitution of Lys11 of the wild-type sequence with Arg in the amino acid sequence of the antagonist, and a substitution of Gly31 of the wild-type sequence with Pro in the amino acid sequence of the antagonist;
- (ii) a truncation of the first two amino acid residues of the antagonist sequence such that it starts at amino acid residue Thr3, a substitution of Lys11 of the wild-type sequence with Arg in the amino acid sequence of the antagonist, a substitution of Gly31 of the wild-type sequence with Pro in the in the amino acid sequence of the antagonist, and a substitution of Pro32 of the wild-type sequence with Gly in the amino acid sequence of the antagonist; and
- (iii) a truncation of the first two amino acid residues of the antagonist sequence such that it starts at amino acid residue Thr3, a substitution of Lys11 of the wild-type sequence with Arg in the amino acid sequence of the antagonist, a substitution of

Thr12 of the wild-type sequence with Ser in the amino acid sequence of the antagonist, a substitution of His13 of the wild-type sequence with Phe in the amino acid sequence of the antagonist, and a substitution of Gly31 of the wild-type sequence with Pro in the in the amino acid sequence of the antagonist.

66 73.

A method of producing the fusion polypeptide of claim 40 comprising:

- (i) introducing the gene fusion a host cell;
- (ii) growing said host cell;
- (iii) accumulating said fusion polypeptide;
- (iv) preparing an extract containing said fusion polypeptide;
- (v) purifying said fusion polypeptide.

67 74.

A method of claim 73, wherein said host cell is selected from the list consisting of bacteria, yeast, fungi, algae, protozoa, plant cells and animal cells.

68 75.

A method of producing the fusion polypeptide of claim 41 comprising:

- (i) introducing the fusion into a host cell;
- (ii) growing said host cell;
- (iii) accumulating said fusion polypeptide;
- (iv) preparing an extract containing said fusion polypeptide;
- (v) purifying said fusion polypeptide.

69 76.

A method of claim 75, wherein said host cell is selected from the list consisting of bacteria, yeast, fungi, algae, protozoa, plant cells and animal cells.

70 77. A method of producing the fusion polypeptide of claim 40 in a plant comprising:

- (i) introducing the gene fusion into said plant;
- (ii) growing said plant;
- (iii) accumulating said fusion polypeptide in said plant;
- (iv) preparing an extract containing said fusion polypeptide;
- (v) purifying said fusion polypeptide.

71 78. A method of producing the fusion polypeptide of 40 in an animal comprising:

- (i) introducing the gene fusion into said animal;
- (ii) growing said animal;
- (iii) accumulating said fusion polypeptide in said animal;
- (iv) preparing an extract containing said fusion polypeptide;
- (v) purifying said fusion polypeptide.

72 79. A method of producing the fusion polypeptide of claim 41 in a plant comprising:

- (i) introducing the gene fusion into said plant;
- (ii) growing said plant;
- (iii) accumulating said fusion polypeptide in said plant;
- (iv) preparing an extract containing said fusion polypeptide;
- (v) purifying said fusion polypeptide.

73 80. A method of producing the fusion polypeptide of 41 in an animal comprising:

- (i) introducing the gene fusion into said animal;

- (ii) growing said animal;
- (iii) accumulating said fusion polypeptide in said animal;
- (iv) preparing an extract containing said fusion polypeptide;
- (v) purifying said fusion polypeptide.

74/ 81. A method to purify the fusion polypeptide of claim 40, wherein supernatant from a cellular extract of a host cell is purified by affinity chromatography, using an affinity handle specific affinity matrix, the polypeptide of claim 4 is cleaved from the affinity handle, dialysed and separated on a affinity handle specific affinity matrix.

75/ 82. A method to purify the fusion polypeptide of claim 41, wherein supernatant from a cellular extract of a host cell is purified using an affinity handle specific affinity matrix, the polypeptide of claim 6 is cleaved from the affinity handle, dialysed and separated on a affinity handle specific affinity column.

76/ 83. The method of claim 81, wherein the affinity handle is a GST fusion protein, the fusion polypeptide is separated from the supernatant using a glutathione-affinity matrix, the polypeptide of claim 4 is cleaved from the affinity handle by thrombin digestion, dialysed against phosphate buffered saline (PBS), and separated on a endotoxin-removal column.

77/ 84. The method of claim 82, wherein the affinity handle is a GST fusion protein, the fusion polypeptide is separated from the supernatant using a glutathione-affinity matrix, the polypeptide of claim 6 is cleaved from the affinity handle by thrombin digestion,

dialysed against phosphate buffered saline (PBS), and separated on an endotoxin-removal column.

78/85.

A pharmaceutical composition comprising a biologically-active amount of one of the novel polypeptides are preferred embodiments of the invention.

79/86.

A compound having a three dimensional structure, wherein the three dimensional structure is capable of high-affinity binding to CXCR1 and CXCR2 receptors in a mammalian inflammatory cell so as to inhibit activation of the inflammatory cell.